

## REMARKS

Claims 27-50 were pending in this application. Claims 28 and 38-43 have been canceled.

The Title of the invention has been amended to describe the subject matter of the invention.

Claim 27 has been amended to recite "radiculopathy." Support for this amendment is found, for example, at page 10, line 10 of the specification, wherein radiculopathy is listed in the definition of "neuropathic pain."

Claim 27 has been amended to delete the terms "preventing" and "prophylactically." Claim 35 has been amended to delete the term "prophylactically."

Claims 27 and 29 have been amended to recite 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline. Support for this amendment is found, for example, at page 14, line 11 of the specification.

Claims 47-50 have been amended to recite specific dosages of the compound of claim 27. Support for these amendments is found, for example, at page 33, lines 5-12.

Claims 29-32, 35, 44, 46 and 47 have been amended to depend from claim 27.

No new matter is added by the amendments. Entry of the amendments and the following remarks is respectfully requested.

### Statement of the Substance of the Interview

Applicant thanks the Examiner for the courtesy extended in the telephonic interview dated May 13, 2009. In response to the Interview Summary mailed May 19, 2009, below is a statement of the substance of the interview.

The undersigned representative of Applicant proposed the above amendment to the claims, in which claim 27 is amended to recite a specific compound, 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline, and a specific condition, radiculopathy. The Examiner indicated that, even though the amendment was outside the scope of the claims as originally examined, such an amendment would be acceptable.

### Claims Rejections under 35 U.S.C. § 103

Claims 27-50 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Man *et al.* (U.S. 6,403,613, "Man") and Ignatowski *et al.* (*Brain Research*, 1999, 841: 70-77, "Ignatowski"). (Office Action, pages 2-3). Applicant respectfully disagrees.

A. The Patent Office has not shown any motivation to select the specific compound and disorder of the instant claims from Man and Ignatowski.

The claims as amended herein recite, *inter alia*, methods of treating radiculopathy using a specific compound, 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline. Applicant requests that the obviousness rejection be withdrawn because art cited by the Examiner does not teach or suggest the specific use of 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline for treating radiculopathy, much less the specific dose of the compound as claimed in claims 46-50.

In the context of claims to biologically active chemical compounds, the Federal Circuit has recently affirmed the requirement that obviousness based on structural similarity must be supported by “identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound...in a particular way to achieve the claimed compound.” *Eisai Co. Ltd. v. Dr. Reddy’s Laboratories, Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008)(citing *Takeda Chemical Ind., Ltd. v. Alphapharm Pty., Ltd.*, 429 F.3d 1350, 1360 (Fed. Cir. 2007) (compounds at issue not *prima facie* obvious over a compound of similar structure because the prior art provided no motivation to modify that compound to arrive at the claimed compounds).

In *Eisai*, the Federal Circuit held that claims to a specific compound, rabeprazole, were not obvious over the prior art’s teaching of a structurally similar compound, lansoprazole. *Eisai*, 533 F.3d at 1359. Rabeprazole and lansoprazole differ only at the 4-position, wherein rabeprazole has a 4-methoxypropoxy group and lansoprazole has a 4-trifluoroethoxy group. *Id.* at 1357. The Court held that even though the prior art taught that lansoprazole had desirable chemical and biological properties and would therefore have been considered a candidate for a lead compound, there was no motivation to modify the structure of lansoprazole in the required way to arrive at rabeprazole. *Id.* Indeed, the Court emphasized that, after the Supreme Court’s decision in *KSR Int’l Co. v. Teleflex Inc.*, the prior art must provide some reason or motivation to make the necessary change in structure in order for a *prima facie* case of obviousness to be made. *Eisai*, 533 F.3d at 1359 (citing *KSR Int’l Co. v. Teleflex Inc.* 127 S.Ct. 1727, 1742 (2007) (necessary to “supply some reasons for narrowing the prior art universe to a ‘finite number of identified, predictable

solutions.”<sup>1</sup>). Thus, Applicant points out that the current law of obviousness in cases concerning structurally similar compounds “requires a showing of ‘adequate support in the prior art’ for the change in structure.” *Takeda*, 429 F.3d at 1356 (*quoting In re Grabiak*, 769 F.2d at 729).

Here, although the instant claims are method claims, they recite the use of a specific compound, such that the law cited above is relevant. Man teaches that certain diseases and disorders may be treated with TNF- $\alpha$  inhibitors, including certain 1-oxo- and 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)isoindolines. (Man, column 4, line 35 to column 5, line 39). Man does not teach or suggest the compound of the claimed methods, nor does Man provide any teaching or suggestion of modifications of the compounds therein that would lead one of ordinary skill in the art to arrive at the compound of the instant claims. Moreover, Man does not teach or suggest the treatment of pain, not to mention the specific disorder of the instant claims—radiculopathy. Thus, Man does not provide one of ordinary skill in the art with any motivation to select a particular compound, then modify that compound to arrive at 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline, much less for the treatment of radiculopathy. *See Eisai*, 533 F.3d at 1357.

Ignatowski does not cure the defects of Man. Ignatowski teaches that neuropathic pain is mediated by TNF, but it does not teach or suggest radiculopathy. (Ignatowski, page 76). Ignatowski does not teach or suggest the use of isoindole compounds, much less 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline, for the treatment of radiculopathy. Thus, like Man, Ignatowski provides no motivation to select 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline for the treatment of radiculopathy as claimed herein. Therefore, the instant claims are not *prima facie* obvious over the cited references.

**B. No reasonable expectation of success exists in combining Man and Ignatowski as required to arrive at the claimed methods.**

The Patent Office has not presented evidence to demonstrate that the specific compound of the claimed methods would be effective in treating radiculopathy. Without such evidence, no reasonable expectation of success exists because a

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<sup>1</sup> In *Takeda*, a post-KSR decision, the Federal Circuit also held that a structurally similar compound was not *prima facie* obvious because the prior art provide no motivation to make the specific change in structure. *Takeda Chemical Ind., Ltd. v. Alphapharm Pty., Ltd.*, 429 F.3d 1350 (Fed. Cir. 2007).


reasonable expectation of success requires more than a motivation to simply “vary all parameters or try each of numerous possible choices until one possibly arrive[s] at a successful result...” *Medichem v. Robaldo*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting *In re O’Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988); see also *KSR*, 127 S.Ct. at 1739 and 1742 (an obviousness determination takes into account whether the combination of elements would yield “anticipated success” or “predictable results”). Furthermore, the courts have long recognized the unpredictability of the biological properties of chemical compounds. See, e.g., *In re Eli Lilly & Co.*, 902 F.2d. 943, 948 (Fed. Cir. 1990) (“we recognize and give weight to the unpredictability of biological properties...”). In view of this knowledge, even considering that Ignatowski generally teaches that inhibition of TNF could be useful in treating pain, one of ordinary skill in the art would not expect that every compound demonstrating TNF- $\alpha$  activity would be useful in treating radiculopathy. Without more specific guidance in the art, no reasonable expectation exists to use the specific compound of the instant methods for the treatment of radiculopathy, much less the specific dose of the compound as provided in claims 46-50. Thus, because the Patent Office has not presented sufficient evidence of a reasonable expectation of success, a *prima facie* case of obviousness has not been made.

### Conclusion

In view of the foregoing, the rejection of the claims should be withdrawn. Reconsideration, entry of the above amendments and remarks and allowance of the pending claims are respectfully requested. Should the Examiner not agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues. No fee is believed to be due with this submission. However, the Commissioner is hereby authorized to charge any required fees under 37 C.F.R. § 1.17, or any other required fee, or any credits, to Jones Day Deposit Account No. 503013.

Date: June 9, 2009

Respectfully submitted,

  
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